UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/803,541	03/17/2004	Gary Brodsky	2848-53	6260

22442 7590 05/03/2006

SHERIDAN ROSS PC
1560 BROADWAY
SUITE 1200
DENVER, CO 80202

EXAMINER	
DESAI, ANAND U	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 05/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/803,541	BRODSKY, GARY	
	Examiner	Art Unit	
	Anand U. Desai, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,14-16,23,38-40 and 42-57* is/are pending in the application.

4a) Of the above claim(s) *23 and 42-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,14-16,38-40 and 46-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to Amendment filed on February 15, 2006. Claims 9-13, 18-22, 24-37, and 41 have been cancelled. New claims 46-57 have been added. Claims 1-8, 14-16, 38-40, and 46-57 are currently pending and are under examination. Claims 23, and 42-45 stand finally withdrawn from consideration as drawn to a nonelected invention.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawal of Rejections

3. The rejection of claims 1-8 under 35 U.S.C. § 102(b) as being anticipated by Kilic, F. et al. (Journal of Biological Chemistry, 272(8): 5298-5304 (1997)) is withdrawn.

4. The rejection of claims 38-40 under 35 U.S.C. § 102(b) as being anticipated by Fatkin, D. et al. (IDS document # 6) is withdrawn.

Pending Rejections

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-5, 7, 8, 15, 16, 38-40, 46-48, and 53-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. The claims are drawn to a peptide "consisting essentially of" an amino acid sequence. Applicants definition in the specification and further clarified in the response to the office action mailed October 19, 2005, the peptide would have from at least one, and up to about 20, additional heterologous amino acids flanking each of the C- and/or N-terminal ends of the specified amino acid sequence (see paragraph [0107]), therefore it is unclear how the peptides differ by one substitution of a recited SEQ ID NO: 2 or SEQ ID NO: 4 as claimed in 1(d), 4, 5? Further clarification is requested as to what is encompassed by a fragment that is consisting essentially of a SEQ ID NO?

8. Claims 1-8, 14-16, 38-40, 46-52, and 55-57 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabled for a composition comprising prelamin A (SEQ ID NO: 4) or the prelamin A peptides with the singular modification that affects the formation of normal nuclear lamina structures, and the differentiation of cardiac and skeletal myoblast, does not reasonably provide enablement for isolated complexes comprising **fragments, peptides that differ by at least one substitution, deletion, or insertion, and peptides that are at least 70% identical of SEQ ID NO: 2, and SEQ ID NO: 4** that would affect the formation of normal nuclear lamina structures, and induction of myoblast activation and differentiation.

9. The scope of enablement rejection was disclosed in the office action mailed October 19, 2005.

Response to Remarks

Applicant traverse the rejection of claims under 35 U.S.C § 112, first paragraph, on the basis of enablement. Applicant cites page 19, lines 9-18 of the specification to submit that at the time of the invention, information was available regarding the series of post-translational modifications that result in the processing of prelamin A into lamin A, including the importance of the CAAX motif and cysteine farnesylation. Thus, Applicant states that one of ordinary skill was apprised of where the prelamin A protein is likely or not likely to tolerate modifications. Applicant states Park et al. do not teach that the presence of multiple basic residues just upstream of the CAAX region as necessary or critical for protein binding to farnesyltransferase, rather it simply teaches an enhanced affinity of a CAAX motif for farnesyltransferase. Applicant states that Park et al. further enhances the present specification disclosure that describes what residues in SEQ ID NO: 2 and SEQ ID NO: 4 may be modified to preserve or disrupt activity of the proteins. Applicant cites Xie et al. and Sherrill et al. to show that a functionally analogous yeast protein provides significant information regarding the impact of farnesyl group on the biological activity of yeast pheromone, and therefore would similarly effect the function of SEQ ID NO: 2 in any cell. Applicant cites page 34, line 17 to page 37, line 2 to provide support for the description of the 15 amino acids of SEQ ID NO: 2 that are candidates for modification or not, based on sequence homology with other animal species. Applicant states the present specification provides guidance regarding what residues of prelamin A (SEQ ID NO: 4) are predicted to tolerate modifications or will produce a processing deficient prelamin A protein. Applicant states that modifications at Arg60, Leu85, Arg89, Asn195, Glu203, and Arg377 are shown to negatively impact prelamin A processing and resultant myotube formation and

myoblast differentiation. Applicant states given the guidance provided in the specification and the knowledge in the art, the residues recited in claim 39 near the CAAX processing site could clearly be modified to disrupt prelamin A processing. Applicant states the specification provides sufficient guidance to make and use the claimed proteins, including the claimed homologues and fragments.

Applicant's arguments filed February 15, 2006 have been fully considered but they are not persuasive. Initially, the Xie et al. and Sherrill et al. references, which are to describe the impact of farnesyl group on the biological activity of yeast pheromone protein, are not readily available. The references are missing from the response.

The specification does provide guidance to make prelamin A peptides with single substitutions, wherein the modification encompasses Arg60Gly, Leu85Arg, Arg89Leu, Asn195Lys, Glu203Gly, and Arg377His. The modified prelamin A peptides are stated to differentially affect myocyte morphology. Myotubes expressing the Asn195Lys and Glu203Gly often contain parallel rows of nuclei, and the intercellular organization of the myotubes are arranged at various angles of up to 90 degrees relative to adjacent myotubes, while myotubes expressing Arg377His have a segmented appearance, and the nuclei are not membrane associated as in normal skeletal muscle (see example 3). Thus distinct modifications confer different morphological effects.

The specification does not describe the biological activity of peptides that consist essentially of SEQ ID NO: 2, peptides that are 70% identical to SEQ ID NO: 2, and peptides that differ from SEQ ID NO: 2 by one substitution, deletion or insertion of an amino acid residue for SEQ ID NO: 2. The specification does not describe the therapeutic composition that promotes

myoblast activation and growth or regeneration of cardiac or skeletal muscle, which comprises a fragment of SEQ ID NO: 4, or an amino acid sequence that is at least 70% identical to SEQ ID NO: 4. Therefore, experimentation left to those of ordinary skill in the art to make and use the peptides having the desired biological would be improperly extensive and undue.

10. Claims 1-5, 7, 8, 14-16, 38, 39, 46, 47, 48, 49, 50, 51, 55, 56, and 57 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

11. The written description rejection was disclosed in the office action mailed October 19, 2005.

Response to Remarks

Applicant traverse the rejection of claims under 35 U.S.C § 112, first paragraph, written description. Applicant states the specification provides detailed guidance regarding which amino acids in the polypeptides can be altered without affecting the function of the specific polypeptide. Applicant cites page 34, line 17 to page 37, line 2 to describe which of each of the positions of the 15 amino acid sequence of SEQ ID NO: 2 are candidates for modification, based on sequence homology with other animal species. Applicant states that one of skill in the art can readily envision the proteins encompassed by claims 14-16, and 38-39. Applicant states the specification has taught which residues are most important to the function of prelamin A function by noting residues that are important with respect to the processing site and by identifying

residues that, if modified, can render the prelamin A processing-deficient. Applicant states that with regard to claim 38, the specification provides a specific identification of several residues that could be targeted to disrupt prelamin A processing, and further provides working examples illustrating that several of these positions result in a processing-deficient prelamin A protein. Applicant states the rejection of claim 39 is completely unclear, since this claim specifically recites sites for modification in prelamin A, several of which are shown by the specification to affect prelamin A processing and the functions associated with this processing that have been discovered by the present inventor.

Applicant's arguments filed February 15, 2006 have been fully considered but they are not persuasive. In regards to claims drawn to SEQ ID NO: 2, the disclosure does not describe the biological activity of SEQ ID NO: 2. The disclosure does not describe biologically active deletion peptides of SEQ ID NO: 2, either consisting essentially of an amino acid sequence that is at least 70% identical to SEQ ID NO: 2 or that differ from SEQ ID NO: 2 by one substitution, deletion, or insertion of an amino acid residue.

In regards to claims drawn to prelamin A (SEQ ID NO: 4), the specification does provide guidance to make prelamin A peptides with single substitutions, wherein the modification encompasses Arg60Gly, Leu85Arg, Arg89Leu, Asn195Lys, Glu203Gly, and Arg377His as disclosed in claim 40. The specification does not describe prelamin A peptides with any amino acid substitutions in the residues as disclosed by claim 39.

Applicant describes in paragraph [0103] the method of identifying a peptide sequence from SEQ ID NO: 4 for inter-nuclear transport, thus the specification does describe the method

of obtaining, but does not describe the possession of fragments of SEQ ID NO: 4 with inter-nuclear transport domain biological activity as disclosed for example in claim 15.

The MPEP 2163 states that the purpose of the written description requirement is to ensure that the inventor had possession, at the time the invention was made, of the specific subject matter claimed. To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., >*Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003);< *Vas-Cath, Inc. v. Mahurkar,* 935 F.2d at 1563, 19 USPQ2d at 1116. Another objective is to put the public in possession of what the applicant claims as the invention. See *Regents of the University of California v. Eli Lilly,* 119 F.3d 1559, 1566, 43 USPQ2d 1398, 1404 (Fed. Cir. 1997), cert. denied, 523 U.S. 1089 (1998).

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.")

Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the modified peptide as currently claims, and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 102

12. Claims 38, and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Barton and Worman (Journal of Biological Chemistry 274(42): 30008-30018 (1999)).

Barton and Worman disclose the expression of a prelamin A fragment consisting of amino acid residues 389-664, wherein the cysteine at position 661 is modified to serine (see page 30008, Experimental Procedures, Plasmid construction section, page 30010, In Vitro Binding and Prenylation Assays, page 30013, Results, Binding assays confirm that Narf specifically binds to preAct section, and Figure 5A, lane 2).

13. Claims 38, 39, 40, and 53-57 are rejected under 35 U.S.C. 102(b) as anticipated by Őstlund et al. (Journal of Cell Science 114(24): 4435-4445 (2001)).

Őstlund et al. disclose the recombinant expression of FLAG-tagged fusion prelamin A polypeptides, wherein the prelamin A sequence has a singular amino acid substitution. The substitution is located either in the rod domain (N195K). Őstlund et al. do describe the irregular lamin nuclear network upon expression of prelamin A mutant (N195K) (see page 4436, Materials and Methods, Plasmid construction and page 4437, 1st sentence of Results section, and Figures 1, and 7).

Claim Rejections - 35 USC § 102/ Claim Rejections - 35 USC § 103

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 38, 39, 40, and 53-57 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Favreau et al. (Experimental Cell Research 282: 14-23 (2003)).

Favreau et al. disclose the recombinant expression of FLAG-tagged fusion prelamin A polypeptides, wherein the prelamin A sequence has a singular amino acid substitution. The substitution is located either in the carboxy-terminal tail (R453W, R482W) or in the rod domain (N195K) (see page 15, Materials and Methods, Cell culture and transfection and Immunofluorescence microscopy sections). Favreau et al. do describe the irregular lamin nuclear network upon expression of prelamin A mutant (N195K) (see page 19-20, Discussion, particularly reference to rod domain mutant). Favreau et al. do not explicitly disclose the isolation of N195K, but it would have been obvious the person having ordinary skill in the art to isolate the FLAG-tagged protein using the anti-FLAG antibody described by Favreau et al.

Conclusion

17. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

April 26, 2006

JON WEBER
SUPERVISORY PATENT EXAMINER